

AD-A100 411 ARMY ENVIRONMENTAL HYGIENE AGENCY ABERDEEN PROVING GR--ETC F/8 6/20
TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)
JUN 81 M J TOPPER, J 6 HARVEY
UNCLASSIFIED USAEHA-75-51-0160-81 USAEHA-75-51-0163-81 NL

1 OF 1
AD A
100-41

1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	----

END
DATE
FILMED
7-81
DTIC

LEVEL 11

12



UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010

6

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENTS
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. ~~75-51-0160-81~~, ~~75-51-0162-81~~ thru
~~75-51-0165-81~~, ~~75-51-0167-81~~, and ~~75-51-0168-81~~
OCTOBER 1978 - APRIL 1981.

AD A100411

A
E
H
A

Handwritten notes and stamps, including "EHA-81", "A", and "JUN 25 1981".

Approved for public release, distribution unlimited.

Handwritten notes and stamps, including "11-11-81" and "1-1-81".

038150

81 6 18 026

DTC FILE COPY

Unclassified

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 75-51-0160, 0162 thru 0165, 0167, and 0168-81	2. GOVT ACCESSION NO. <i>h-1</i>	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Topical Hazard Evaluation Program of Candidate Insect Repellents, US Department of Agriculture Proprietary Chemicals, Study Nos. 75-51-0160-81, 75-51-0162-81 thru 75-51-0165-81, 75-51-0167-81, and 75-51-0168-81, Oct 78 - Apr 81	5. TYPE OF REPORT & PERIOD COVERED Final, Oct 78 - Apr 81	
7. AUTHOR(s) MICHAEL J. TOPPER, CPT, VC JOHN G. HARVEY	6. PERFORMING ORG. REPORT NUMBER	
9. PERFORMING ORGANIZATION NAME AND ADDRESS US Army Environmental Hygiene Agency Aberdeen Proving Ground, MD 21010	8. CONTRACT OR GRANT NUMBER(s)	
11. CONTROLLING OFFICE NAME AND ADDRESS Commander US Army Health Services Command Fort Sam Houston, TX 78234	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS	
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)	12. REPORT DATE Oct 78 - Apr 81	
	13. NUMBER OF PAGES 7	
	15. SECURITY CLASS. (of this report) Unclassified	
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE	
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release; distribution unlimited.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)		
18. SUPPLEMENTARY NOTES		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number)		
AI3-37330a	AI3-37346a	Skin irritation
AI3-37339a	AI3-37349a	Eye irritation
AI3-37350a	Photoirritation	Topical Hazard Evaluation Program
AI3-37332a	ALD	USDA Proprietary Chemicals
AI3-37343a	Guinea pig sensitization	
20. ABSTRACT (Continue on reverse side if necessary and identify by block number)		
Preliminary hazard evaluation of the above candidate insect repellent chemicals were performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. Chemicals AI3-37330a, 37339a, and 37350a were noninjurious to the eyes of rabbits. Chemicals AI3-37332a, 37343a, 37346a, and 37349a caused mild injury to the cornea and, in addition, some injury to the conjunctiva. All of the chemicals did not cause skin or photoirritation, and did not prove to be skin sensitizers. Chemicals AI3-37343a and 37349a were moderately toxic by ingestion. The remaining chemicals were relatively nontoxic by ingestion. It was recommended that all chemicals be approved for further testing as candidate insect repellents.		

DD FORM 1 JAN 73 1473

EDITION OF 1 NOV 65 IS OBSOLETE

Unclassified

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)



DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

CPT Topper/lm/AUTOVON
584-3627

11 JUN 1981

REPLY TO
ATTENTION OF

HSE-LT-T/WP

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents,
US Department of Agriculture Proprietary Chemicals, Study Nos.
75-51-0160-81, 75-51-0162-81 thru 75-51-0165-81, 75-51-0167-81, and
75-51-0168-81, October 1978 - April 1981

Executive Secretary
Armed Forces Pest Management Board
Forest Glen Section, WRAMC
Washington, DC 20012

A summary of the pertinent findings and recommendations of the inclosed report follows:

Preliminary hazard evaluations of the above candidate insect repellent chemicals were performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. Chemicals AI3-37330a, 37339a, and 37350a were noninjurious to the eyes of rabbits. Chemicals AI3-37332a, 37343a, 37346a, and 37349a caused mild injury to the cornea and, in addition, some injury to the conjunctiva. All of the chemicals did not cause skin or photoirritation, and did not prove to be skin sensitizers. Chemicals AI3-37343a and 37349a were moderately toxic by ingestion. The remaining chemicals were relatively nontoxic by ingestion. It was recommended that all chemicals be approved for further testing as candidate insect repellents.

FOR THE COMMANDER:

1 Incl
as (5 cy)

John F. Mazur
JOHN F. MAZUR
MAJ, MSC

Director, Laboratory Services

CF:
HQDA (DASG-PSP)
Cdr, HSC (HSPA-P)
Dir, Advisory Cen on Tox, NRC
Comdt, AHS (HSA-IPM)
USDA, ARS (Dr. Terrence McGovern)
USDA, ARS-Southern Region (2 cy)

Approved for	☒
Disapproved	☐
Comments	

A



REPLY TO
ATTENTION OF

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

HSE-LT-T/WP

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENTS
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0160-81, 75-51-0162-81 thru
75-51-0165-81, 75-51-0167-81, and 75-51-0168-81
OCTOBER 1978 - APRIL 1981

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, Florida, 13 October 1978.

b. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of the Army, Office of The Surgeon General; the Armed Forces Pest Control Board; and the US Department of Agriculture, Agricultural Research, Science and Education Administration, titled, Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCE. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), 1972, revised 1976.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of candidate insect repellents: AI3-37330a, 37332a, 37339a, 37343a, 37346a, 37349a and 37350a.

4. SUMMARY OF FINDINGS. Hazard evaluations of the above-named candidate repellents were conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study, and Sprague-Dawley rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed by this Agency follows:*†

* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education, and Welfare Publication No. (NIH) 74-23, revised 1978.

† The experiments reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

Approved for public release, distribution unlimited.

Study Nos. 75-51-0160-81, 75-51-0162-81 thru 75-51-0165-81, 75-51-0167-81, and 75-51-0168-81, Oct 78-Apr 81

TABLE. PRESENTATION OF DATA

Test	Results	Interpretation	
<u>SKIN IRRITATION STUDIES</u>			
<u>Rabbits</u>			
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	All tested chemicals did not cause any irritation of the intact skin or of the skin surrounding an abrasion.	USAEHA Category I (ref Appendix A)	
0.5-mL technical grade chemical applied to each of six rabbits.			
<u>EYE IRRITATION STUDIES</u>			
<u>Rabbits</u>			
Single 24-hour application of 0.1-mL technical grade chemical to one eye of each of six New Zealand White rabbits.	Chemicals AI3-37330a, 37339a, and 37350a did not cause any irritation to the eyes of rabbits.	USAEHA Category A (ref Appendix A)	
	Chemicals AI3-37332a, 37343a, 37346a, and 37349a caused mild injury to the cornea and, in addition, some injury to the conjunctiva.	USAEHA Category C (ref Appendix A)	
<u>APPROXIMATE LETHAL DOSE (ALD)</u>			
<u>Oral</u>			
Rats (male)-no diluent	AI3-37330a	1272 mg/Kg	These chemicals are relatively nontoxic by ingestion.
	AI3-37332a	1270 mg/Kg	
	AI3-37339a	1916 mg/Kg	
	AI3-37346a	1900 mg/Kg	
	AI3-37350a	9701 mg/Kg	
	AI3-37343a	851 mg/Kg	These chemicals are moderately toxic by ingestion.
	AI3-37349a	851 mg/Kg	

Study Nos. 75-51-0160-81, 75-51-0162-81 thru 75-51-0165-81, 75-51-0167-81, and 75-51-0168-81, Oct 78-Apr 81

Test	Results	Interpretation
<u>PHOTOCHEMICAL SKIN IRRITATION STUDIES</u>		
<u>Rabbits</u>		
A single 0.05-mL application of a 25-percent (w/v) solution of each chemical and a 10 percent (w/v) Oil of Bergamot solution (positive control) in 95-percent ethyl alcohol were applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes at a distance of 10-15 cm.	A 25-percent solution of each tested chemical in ethanol did not cause a photochemical irritation reaction under test conditions.	All tested chemicals did not cause a photochemical irritation reaction under test conditions and are not expected to cause a photochemical irritation in humans.
<u>Control</u>		
Following UV exposures of the rabbits, 0.05 mL of test chemical, positive control, and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation at 24, 48, and 72 hours.	Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.	

Study Nos. 75-51-0160-81, 75-51-0162-81 thru 75-51-0165-81, 75-51-0167-81, and 75-51-0168-81, Oct 78-Apr 81

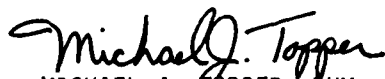
Test	Results	Interpretation
<u>SENSITIZATION STUDIES</u>		
<u>Guinea Pigs (Male)</u>		
Intradermal injections of 0.1 mL of a 0.1-percent solution (w/v) of the tested chemicals or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs for each chemical were given 10 sensitizing doses over a 3-week period. After 2 weeks rest, they were challenged with ID injections of each test chemical.	Challenge doses of the tested chemicals did not produce a sensitization reaction.	The tested chemicals did not produce sensitization reactions under test conditions and are not expected to produce sensitization reactions in man.
Ten positive control guinea pigs were sensitized over 3 weeks with DNCB. After 2 weeks' rest, they were challenged with ID injections of DNCB.	Challenge dose of DNCB in positive control guinea pigs produced a marked sensitization reaction in 10 out of 10 guinea pigs.	DNCB produced a marked reaction, indicating the guinea pigs respond to sensitizing agents.

* A known skin sensitizer.

Study Nos. 75-51-0160-81, 75-51-0162-81 thru 75-51-0165-81, 75-51-0167-81,
and 75-51-0168-81, Oct 78-Apr 81

5. CONCLUSION. Technical grade chemicals AI3-37330a, 37339a, and 37350a did not cause any skin, eye, or photoirritation, no sensitization reaction, and did not prove to be an acute ingestion hazard. Technical grade chemicals AI3-37332a, 37343a, 37346a, and 37349a did not cause any skin or photoirritation, no sensitization reaction, and did not prove to be an acute ingestion hazard, but did cause mild injury to the cornea and, in addition, some injury to the conjunctiva.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that the following USDA proprietary chemicals be approved for further testing as candidate insect repellents: AI3-37330a, 37332a, 37339a, 37343a, 37346a, 37349a, and 37350a.



MICHAEL J. COPPER, DVM
CPT, VC
Laboratory Animal Veterinary Officer
Toxicology Division



JOHN G. HARVEY, JR.
Biological Laboratory Technician
Toxicology Division

APPROVED:



ARTHUR H. MCCREESH, Ph.D.
Chief, Toxicology Division

Study Nos. 75-51-0160-81, 75-51-0162-81 thru 75-51-0165-81, 75-51-0167-81, and 75-51-0168-81, Oct 78-Apr 81

APPENDIX A

TOPICAL HAZARD EVALUATION PROGRAM DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.

Study Nos. 75-51-0160-81, 75-51-0162-81 thru 75-51-0165-81, 75-51-0167-81, and 75-51-0168-81, Oct 78-Apr 81

APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following with regard to Topical Hazard Evaluation Program of Candidate Insect Repellents, US Department of Agriculture Proprietary Chemicals, Study Nos. 75-51-0160-81, 75-51-0162-81 thru 75-51-0165-81, 75-51-0167-81, and 75-51-0168-81, October 1978 - April 1981

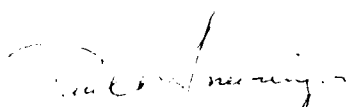
a. This study was conducted in accordance with:

(1) Standing Operating Procedures developed by the Toxicology Division, USAEHA.

(2) Title 21, Code of Federal Regulations, 1980 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratories Studies.

b. Facilities were inspected during its operational phase to insure compliance with paragraph a.

c. The information presented in this report accurately reflects the raw data generated during the course of conducting the study.


PAUL V. SNEERINGER, Ph.D.
Chief, Analytical Quality
Assurance Office

LMED
-18